

Amendments to the Drawings:

The drawing sheets attached in connection with the above-identified application containing Figures 1, 2 and 4 are being presented as a new formal drawing sheets to be substituted for the previously submitted drawing sheets.

Figures 1, 2 and 4 have been amended, figures 3 and 5-8 are not amended. Appended to this amendment are three sheets of Replacement Formal Drawings containing Figures 1, 2 and 4. The specific changes which have been made to Figures 1, 2 and 4 are the inclusion of (SEQ ID NOs) where appropriate.

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following remarks.

I. Status of the Claims

Claims 1-17 are currently pending in the application, with claims 1 and 13 being the independent claims.

Claims 1-6, 8, 12-13 and 15 are currently amended. Claim 1 is amended to delete the term “engineered”, specify that the claimed method detects both known and unknown DNA mutations, single nucleotide polymorphisms, and insertions and deletions, and clarify that the replicates have at least 50% substitutions in at least one of the four DNA bases. Claim 2 is amended to clarify that the substitutions are nucleotide equivalents. Claims 3-4 are amended to specify that the replicates have 70% (claim 3) and 100% substitutions (claim 4), respectively, in at least one of the four DNA bases. Support for the amendment to claims 1-4 can be found, *inter alia*, in paragraphs [0012], [0019], [0040], [0041] and [0132] of the published patent application.

Further, claims 5-6 are amended to specify that the incubation is at 55°C. Support for the amendment to claims 5-6 can be found, *inter alia*, in Example 1 of the specification.

Additionally, claim 12 is amended to recite a proper Markush group and claim 13 is amended to specify that the kit is for the detection in a given DNA sequence of known and unknown DNA mutations, single nucleotide polymorphisms, and insertions and deletions, and comprises nucleotide equivalents. Support for the amendment to claims 12-13 can be found, *inter alia*, in paragraphs [0039], and [0012], [0019], [0050] and [0028], respectively, of the published patent application.

Finally, claim 6 is amended to replace the phrase “of the nature” with the phrase “having the formula”, and claim 15 is amended to correct a typographical error.

II. Information Disclosure Statement

The Office Action, at page 2, states that the listing of references in the specification is not a proper information disclosure statement.

Applicants respectfully state that listings of all references cited in the specification were submitted in two separate Information Disclosure Statements on Forms PTO/SB/08 filed with the U.S. Patent and Trademark Office on December 30, 2005, and March 21, 2006, respectively. The listed documents have been considered by the Examiner, and initialed copies of Forms PTO/SB/08 have been returned to Applicants with the Non-Final Office Action dated November 14, 2006.

III. The Objections to the Specification

The Office Action at page 2 objects to the title of the invention as allegedly being not descriptive, and to the specification, for allegedly lacking the "Brief Description of the Drawings" subtitle. Further, the Office Action objects to the abstract of the disclosure because of the inclusion of legal phraseology.

The foregoing submits a title that is clearly indicative of the claimed invention, and amends the specification to insert the "Brief Description of the Drawings" subtitle. Further, the abstract is amended to eliminate legal phraseology. Accordingly, the objections to the specification are moot and their withdrawal is respectfully requested.

IV. Sequence Compliance

The Office Action, at page 3, objects to the application for allegedly failing to comply with the requirements of 37 CFR §§ 1.821-1.825, and asserts that page 9 and Figures 1-7 in the specification contain sequences which are not identified by sequence identifiers.

The foregoing amendment introduces sequence identifiers for the sequences at page 9, and provides Replacement Formal Drawings for Figures 1, 2 and 4 containing sequence identifiers for the sequences illustrated in the figures. It is respectfully submitted that Figure 5 contains no sequences, and Figures 3, 6 and 7 contain sequence fragments which

cannot be identified by sequence identifiers. Accordingly, the objection is moot and its withdrawal is respectfully requested.

V. The Objections to the Claims

The Office Action, at pages 3-4, objects to claims 1 and 15 for allegedly containing misspellings, and to claim 8 for the misuse of parentheses. The foregoing corrects the misspellings in claims 1 and 15, and the parenthesis in claim 8. These objections are therefore moot and their withdrawal is respectfully requested.

VI. The Rejections Under 35 U.S.C. § 112, Second Paragraph

The Office Action, at pages 4-5, rejects claims 1-17 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. According to the Office Action, the meaning of the phrases “engineered polymerase”, “not natural base” and “of the nature” is not clear. Further, the Office Action states that the term “elevated temperature” is a relative term, which renders the claims indefinite. Applicants respectfully traverse this ground of rejections.

Solely to advance prosecution, and not in acquiescence with the rejections, the foregoing amends the pending claims to delete the terms “engineered”, “non natural base” and “of the nature”, and recite a specific temperature for the cleaving step in claims 5-6. Accordingly, the rejections under 35 U.S.C. § 112, second paragraph, are moot and their withdrawal is respectfully requested.

VII. The Rejections Under 35 U.S.C. § 112, First Paragraph

The Office Action, at pages 5-6, rejects claim 12 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office Action states that there is no support in the specification for the use of both MALDI and ESI

together, and alleges that the amendment to claim 12 filed on December 30, 2005, constitutes new matter.

The foregoing amends claim 12 to recite a Markush group in proper form. Accordingly, this rejection is moot and its withdrawal is respectfully requested.

VIII. The Rejection Under 35 U.S.C. § 102(b)

The Office Action, at pages 6-8, rejects claims 1-17 under 35 U.S.C. § 102(b), as allegedly being anticipated by U.S. Patent No. 6,566,059 B1 to Stanton Jr. *et al.* ("Stanton"). The Office Action states that Stanton discloses methods for the detection in a DNA sequence of DNA mutations, single nucleotide polymorphisms and insertion and deletions. Applicants respectfully traverse this ground of rejections.

1. Summary of the Claimed Invention

The presently claimed invention is directed to a method for the detection in a DNA sequence of known and *unknown* DNA mutations, single nucleotide polymorphisms, and insertions and deletions comprising the steps of: a) producing replicates with a polymerase of the DNA sequence having at least 50% substitutions in at least one of the four DNA bases; b) using the substitutions to cleave the replicates and produce a DNA product presenting sequence-specific fragments; c) analyzing the sequence-specific fragments by mass spectrometry to get sequence-specific fragment patterns; and d) using the sequence-specific fragment patterns to identify sequence changes relative to a reference to the DNA sequence.

Further, the invention is drawn to a kit for the detection in a DNA sequence of known and *unknown* DNA mutations, single nucleotide polymorphisms, and insertions and deletions, comprising: a DNA polymerase, a set of nucleotide equivalents, and a buffer.

2. The Cited Reference Fails to Teach Every Element of the Claimed Invention

Stanton discloses a method for detecting a variance in a nucleotide sequence suspected to contain a *known polymorphism or mutation*. See claims 1, 22, 56 and 65.

Stanton fails to teach a method for detecting *unknown* DNA mutations, single nucleotide polymorphisms, and insertions and deletions, as claimed in the present application.

Additionally, Stanton fails to disclose a kit for the detection in a DNA sequence of known and *unknown* DNA mutations, single nucleotide polymorphisms, and insertions and deletions, comprising a DNA polymerase, a set of nucleotide equivalents, and a buffer. Accordingly, this rejection is improper, and its withdrawal is respectfully requested.

CONCLUSION

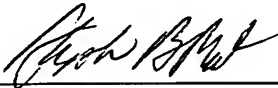
All of the stated grounds of objections and rejections have been properly traversed or rendered moot. Therefore, the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By 

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